DEPARTMENT OF BIOTECHNOLOGY

BIOSYNTHESIS OF PURINES AND PYRIMIDINES: SALVAGE PATHWAY

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WHAT IS BIOSYNTHESIS?

- Biosynthesis is a multistep, enzyme-catalyzed process where substrates are converted into more complex products in living organisms.

- In biosynthesis, simple compounds are modified, converted into other compounds, or joined together to form macromolecules.

PURINES AND PYRIMIDINES

PURINES

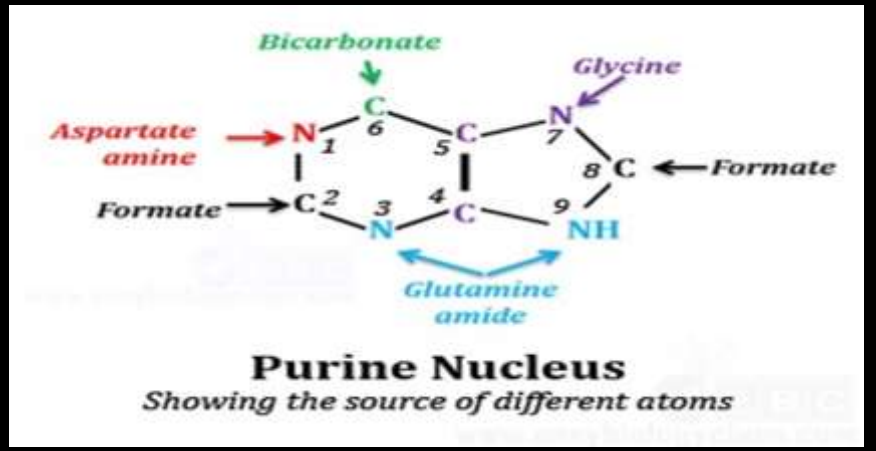
- Purines consist of six-membered and five-membered nitrogen-containing rings, fused together.
- Purine is water soluble.
- Purine are found in high concentration in meat & meat products, especially internal organ such as liver & kidney.
- There are 4 purines:

1.Adenine=6-amino purines

2.Guanine=2-amino-6-oxy purines

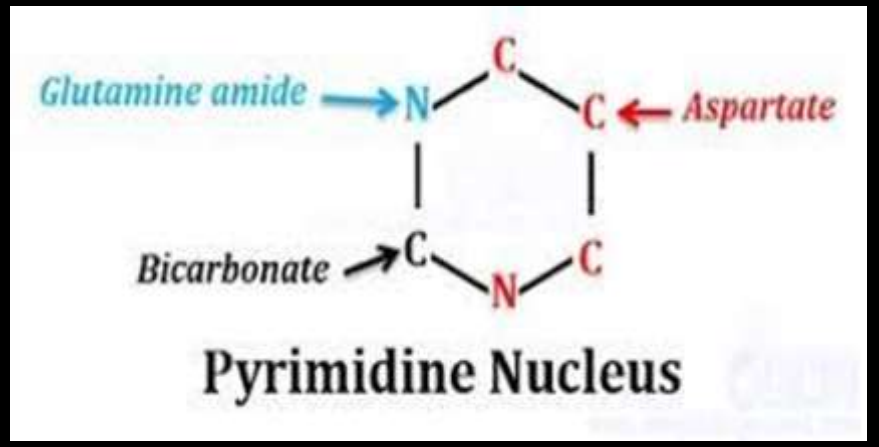
3.Hypoxanthine=6-oxy purines

4.xanthine=2,6-dioxypurines



- Adenine and guanine are found in both DNA and RNA.
- Hypoxanthine and xanthine are not incorporated into the nucleic acids as they are being synthesized but are important intermediates in the synthesis and degradation of the purines nucleotide.

PYRIMIDINES

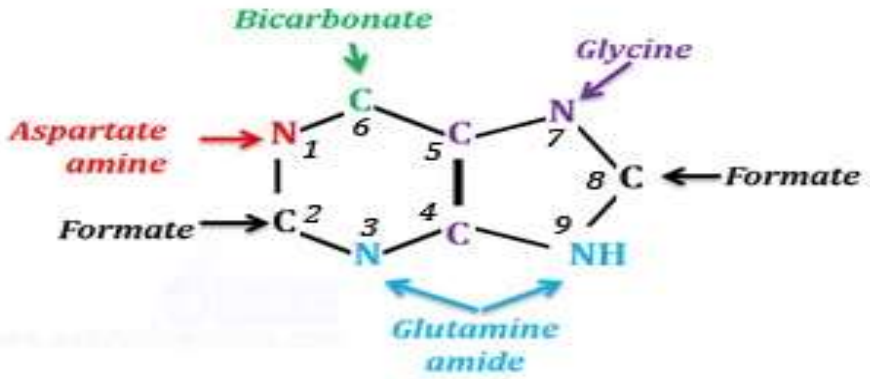


- pyrimidines have only a six membered nitrogen containing ring.
  - There are 3 pyrimidines:

1. Uracil
2. Thymine
3. Cytosine

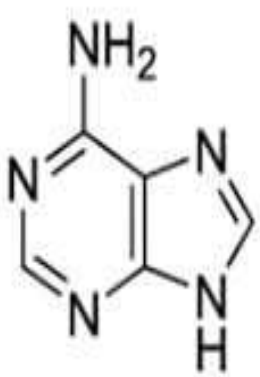
- Cytosines are found in both DNA and RNA
- Uracil is found only in RNA.
- Thymine is normally found in DNA. Sometimes tRNA will contain some thymine as well as uracil.
- The pyrimidine ring is synthesized as free pyrimidine & it is incorporated into the nucleotide.
- Aspartate, glutamine (amide group) & CO_2 contribute to atoms in the formation of pyrimidine ring.

STRUCTURES OF PURINE AND PYRIMIDINE

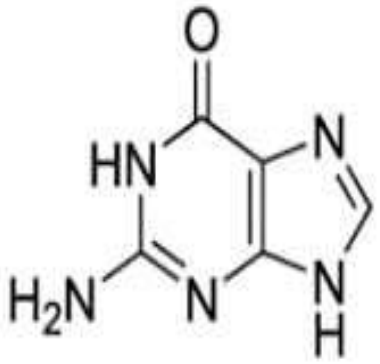


Purine Nucleus

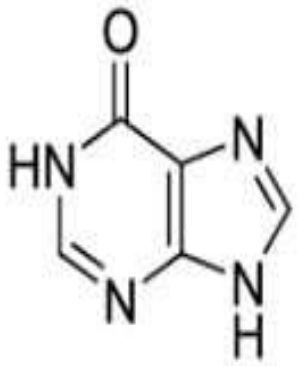
Showing the source of different atoms



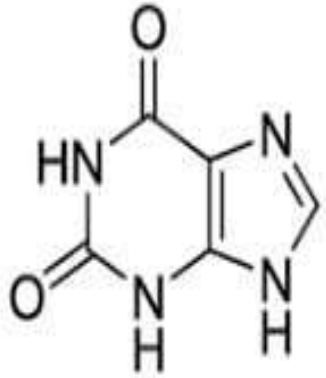
Adenine



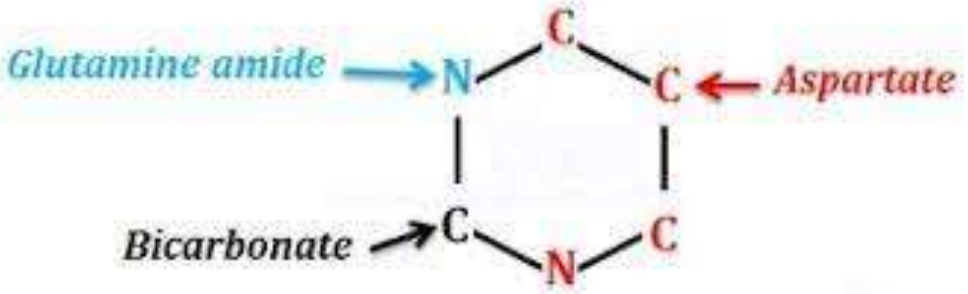
Guanine



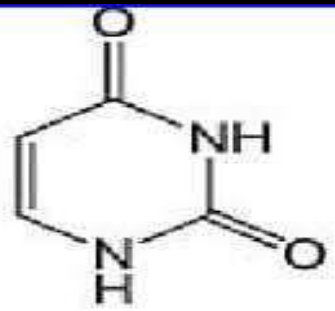
Hypoxanthine



Xanthine



Pyrimidine Nucleus



uracil

cytosine

thymine

PATHWAYS

- There are two pathways for the synthesis of purines and pyrimidines:

1.De-novo synthesis: Biochemical pathway where nucleotides are synthesized from new simple precursor molecules.

2.salvage pathway: used to recover bases and nucleotides formed during the degradation of DNA and RNA.

SALVAGE PATHWAY

- Conversion of free purine to nucleotide is called salvage pathway; where salvage means property saved from losses.
- Metabolic degradation of nucleic acids produces purine bases like adenine, guanine etc.
- This pathway is simpler and consumes very less energy.
- Phosphoribosyl pyrophosphate(PRPP) is the starting materials in this pathway.
- This pathway is found in such tissues which are incapable of synthesis of nucleotide by De-novo method like in brain and RBCs.
- APRT and HGPRT is responsible for most of recycling.

❖ WHY DO WE NEED TO DO SALVAGE PATHWAY?
❖ WHY CELLS ARE INVOLVED IN THIS PATHWAY?

- Because de-novo synthesis require lots of reactions, many ATPs are needed, it is time consuming process, energy consuming process.
- That is why most of our cells they also depend on salvage pathway.

❖ WHAT IS THE ADVANTAGE OF SALVAGE PATHWAY?

- In these salvage pathway, cells try to reutilise the purine bases coming from cell turnover process. So whenever the cell turnover occur so then breakdown of DNA and RNA, so then the bases are released.
- Our cells are going to use these molecules if there is need for new DNA or new RNA synthesis.
- If there is no need these bases are degraded into there metabolic end product like
- purines are degraded into uric acid,
- Pyrimidines are degraded into Co2, ammonia, and in other water soluble products.

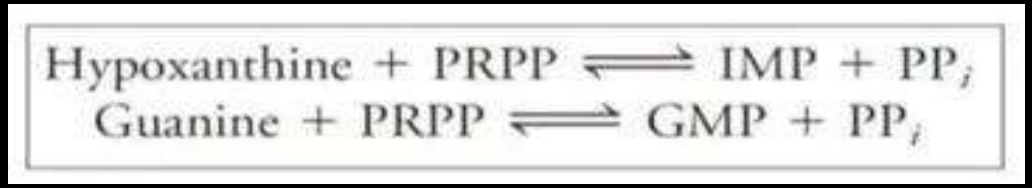
SALVAGE PATHWAY OF PURINE BIOSYNTHESIS

- Purines can be generated in the cells by salvage pathways.
- Liver is the major site for purines nucleotides synthesis.
- Turnover of nucleic acids (particularly RNA) in most cells releases adenine, guanine, and hypoxanthine
- These free purines are reconverted to their corresponding nucleotides through salvage pathways.

➢ Salvage pathway of Purines

- Purines are salvaged by two different enzymes in mammals:
- Adenine phosphoribosyl transferase (APRTase) catalyses the formation of AMP(adenine mono phosphate) from adenine using PRPP.

- Hypoxanthine-guanine phosphoribosyl transferase (HGPRTase), which catalyses the analogous reaction for both hypoxanthine and guanine to IMP(inosine mono phosphate) and GMP(guanine mono phosphate).



Salvage Pathway for Purines.

Nitrogen base + Ribose + Phosphate → Nucleotide.

↓

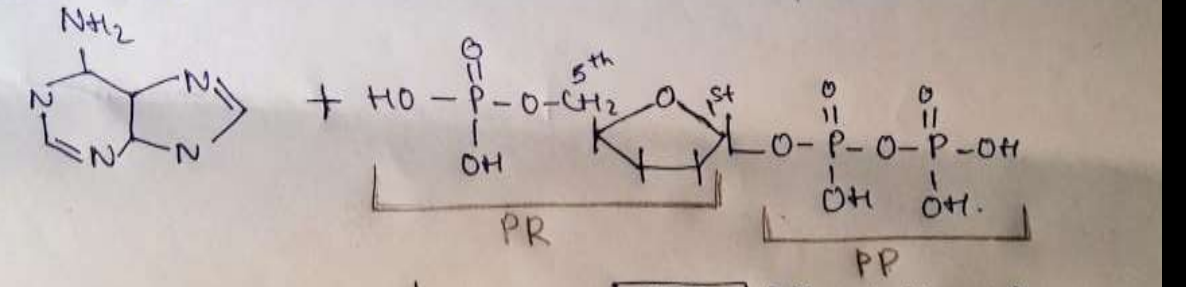
Purine

Pyrimidine

Purines

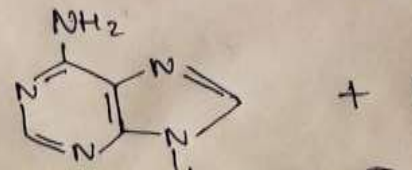
- Adenine
- Guanine
- Hypoxanthine

Adenine → N.B



PRPP (Phosphoribosyl Pypro Phosphate)

↓ APRT (Adenine Phosphoribosyl Transferase)

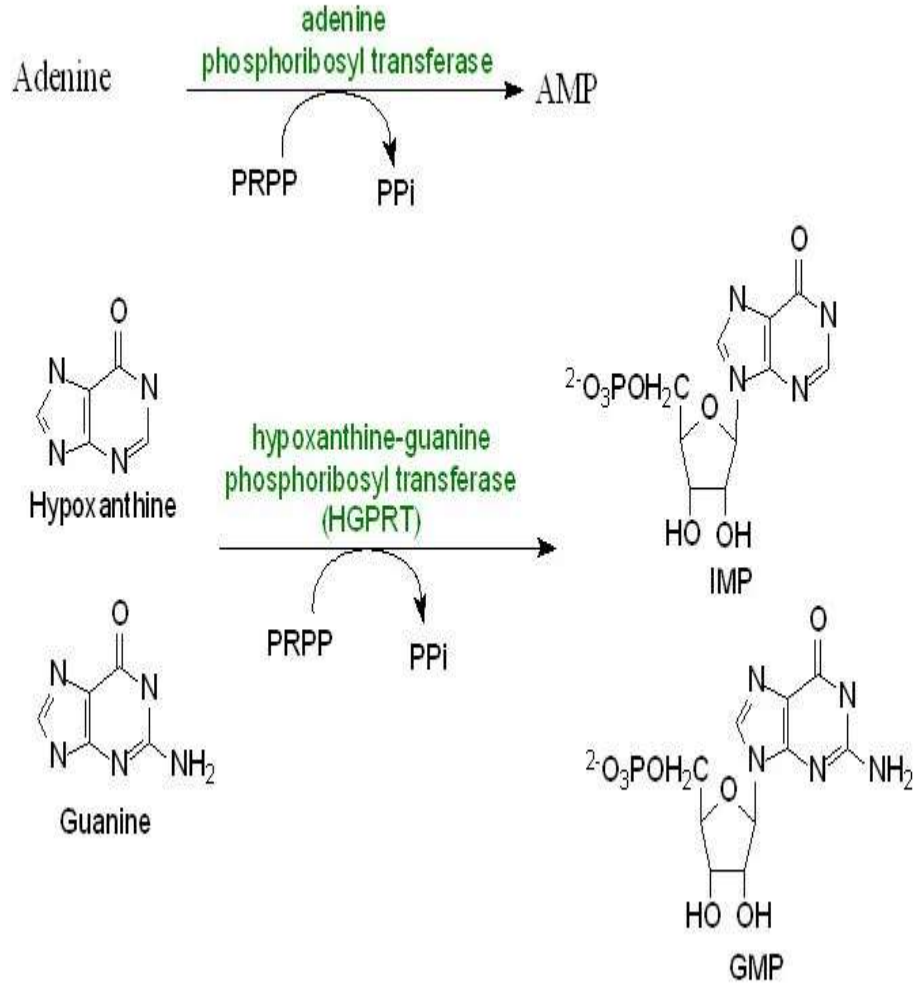


+ PPi

Ribose – 5 – (P)

Nucleotide AMP

Purine Salvage Pathway



Absence of activity of HGPRT leads to Lesch-Nyhan syndrome.

SALVAGE PATHWAY OF PYRIMIDINE BIOSYNTHESIS

- Similar to purines, pyrimidines are also recovered from the derivative intermediates of nucleic acids such as DNA and RNA.
- The recoveries of pyrimidines are catalysed by the enzyme pyrimidine phosphoribosyl transferase.
- Pyrimidine phosphoribosyl transferase enzyme utilizes PRPP as the source of ribose-5-phosphate

SALVAGE OF PYRIMIDINES

Uracil + Ribose -1-phosphate —(Uridine phosphorylase)→ Uridine + Pi

Cytosine + Ribose -1-phosphate —(Cytidine phosphorylase)→ Cytidine + Pi

Thymine + Deoxyribose 1 phosphate —(Thymidine phosphorylase)→ Thymidine + Pi

Uridine or Cytidine + ATP —(Uridine-Cytidine Kinase)→ UMP Or CMP + ADP

Thymidine + ATP —(Thymine Kinase)→ TMP + ADP